PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P35262WO/NCB	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/03529	International filing date *(day/month/year)* 13.08.2003	Priority date *(day/month/year)* 13.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K39/395		
Applicant HAPTOGEN LTD ET AL.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 13 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 14 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11.03.2004	21.12.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Covone-van Hees, M.G Telephone No. +31 70 340-4416

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/03529

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-45 as originally filed

Sequence listings part of the description, Pages

1-4 as originally filed

Claims, Numbers

1-33 received on 24.11.2004 with letter of 22.11.2004

Drawings, Sheets

1/12-12/12 as originally filed

2. With regard to the **language,** all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority in written form.

   ☒ furnished subsequently to this Authority in computer readable form.

   ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-10,17,18 (as to I.A.)

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1-10,17,18 (as to I.A.)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-33
	No:	Claims	
Inventive step (IS)	Yes:	Claims	33
	No:	Claims	1-32
Industrial applicability (IA)	Yes:	Claims	11-16,19-33
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-10,17,18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item IV

Lack of unity of invention

This Authority considers that there are 3 inventions covered by the claims indicated as follows:

I: Claims 2-4,20-22,33 (completely) 1,6-19,24-32 (partially) directed to an antibody according to claim 20-22 (binding to homoserine), and related method for the treatment of a bacterial infection, method of screening, pharmaceutical composition, kit, use in medicine and medicament.

II: Claims 5,23 (completely) 1,6-19,24-32 (partially) directed to an antibody according to claim 23 (binding to peptide thiolactone), and related method for the treatment of a bacterial infection, method of screening, pharmaceutical composition, kit, use in medicine and medicament.

III: Claims 1,6-19,24-32 (all partially) directed to an antibody binding to (Pro)-AI-2, and related method for the treatment of a bacterial infection, method of screening, pharmaceutical composition, kit, use in medicine and medicament.

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

A priori the common linking special technical feature may be seen as the binding specificity of the monoclonal antibody used in the method of treatment, namely directed to lactone (homoserine, peptide thiolactone and (Pro)-AI-2) signal molecules secreted by bacteria.

However, at the priority date of the present application WO0194543 discloses the production of polyclonal antibodies (produced in rabbit) specific binding to homoserine lactone. Polyclonal antibodies binding to homoserine lactone have been produced by derivatizing homoserine lactone to allow attachment with other molecules (e.g. carrier molecules) and conjugated to BSA or KLH (see ex.3). The anti-homoserine antibodies are useful to treat bacterial infection (see cl.52,60,61,64-67). The objective remaining problem of the application is to administer antibodies with higher specificity to treat bacterial infection. The solution is the use of

monoclonal antibodies binding to lactone (as specified in claim 1). This solution is not inventive, since monoclonal antibodies can be obtained by routine methods and represent an obvious alternative to polyclonal antibodies, among which the skilled person would select without the exercise of any inventiveness and merely solve a standard problem, i.e. a higher specificity of said antibodies. Therefore the common concept is directly obvious and not inventive.

In conclusion, as no other technical feature can be distinguished which, in the light of the prior art, could be regarded as special technical feature on which an unifying concept for the present inventions could be based, the groups of claims are not linked by common or corresponding special technical features and define 3 different inventions not linked by a single general inventive concept.

The application, hence does not meet the requirements of unity of invention as defined in Rules 13.1 and 13.2 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1: WO 01/94543 A (QUAY STEVEN C ;QUAY ENTPR LLC K (US)) 13 December 2001 (2001-12-13)

D2: DONG Y-H ET AL: "QUENCHING QUORUM-SENSING-DEPENDENT BACTERIAL INFECTION BY AN N-ACYL HOMOSERINE LACTONASE" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 6839, no. 411, 14 June 2001 (2001-06-14), pages 813-817, ISSN: 0028-0836

D3: Maville et al. 1999 PNAS 96:1218-1223

D4: Chen et al. (01-2002) Nature 415:545-549

1.1 The documents D3 and D4 were not cited in the international search report. Copies of the documents are appended hereto.

2 **Art.34 PCT**

2.1 The amendments filed with the International Bureau under Art.34 PCT are in accordance with the requirements of Art.34(2)(b) PCT.

3 **Art. 6 PCT**

3.1 The monoclonal antibody administered in the method according to claim 1 is defined by "binding to the free soluble form of the antigen in the presence of conjugated derivatives thereof". This definition attempts to characterize the monoclonal antibody mainly by a desired property, without providing the technical features necessary to achieve said result. Consequently, this definition lacks clarity in the sense of Art.6 PCT, since it may be seen as the result to be achieved, merely underlying the technical problem, but lacking any technical feature. In present case, this feature is not a distinguish technical feature among which novelty and/or inventiveness can be established.

3.2 The subject-matter of claim 14 (and related use claim 15) attempts to define the product by means of functional features. This definition is only allowable if the invention cannot otherwise be defined without unduly limiting the scope of the claim and the functional definition can be reduced to practice by the skilled person without undue burden, if necessary with reasonable experiments. In present case however the functional feature used to define the solution to the technical problem, is the problem itself. This formulation covers all future solution to the problem, which means: the scope of the claimed invention would not be unduly limited by including technical features of the claimed molecules, since it is clearly not an undue limitation of the claim to eliminate what has not yet been invented

Furthermore, the examination can never with any certainty, ascertain whether or not such claims are ever distinguished over the state of the art, since this would entail testing all know monoclonal antibodies for binding to a lactone signal molecule. Also the public cannot ascertain such a claim. Consequently, the application does not enable the skilled person to carry out the invention over the whole of the claimed area. For these reasons, this definition is unclear and lacks support in the sense of Art.6 PCT.

Examination of invention I:

Claims 2-4,20-22,33 (completely) 1,6-19,24-32 (partially)

4 **NOVELTY** (Art.33(2) PCT)

4.1 The document D1 discloses production of lactone-derived molecules (homoserine derivatives) and polyclonal antibodies (produced in rabbit) binding thereto (see ex. 3). The production monoclonal antibodies and fragments thereof is suggested (see pg.27

l.20 - p.34 l.30). The anti-homoserine antibodies are useful to treat bacterial infection (see cl.52,60,61,64-67) and for diagnosis (see e.g. pg.5 l.14 - pg.6 l.9).

4.2 D2 discloses the use of enzymes which hydrolyse homoserine lactone and reduce bacterial infection (see the whole article).

4.3 The subject-matter of independent claim 1 (and dependent claims 2-4) differs in that a **"monoclonal"** antibody binding to homoserine lactone is administered to treat bacterial infection. In view of the available prior art the subject-matter of claim 1 appears to be novel (Art.33(2) PCT).

4.4 The same arguments cited for claim 1 apply, mutatis mutandis, for the subject-matter of independent claims 10,11,15-17,28,29-31 referring to a use or compositions comprising said monoclonal antibody and independent claims 14,19,32,33 referring to a monoclonal antibody binding to homoserine lactone, which is therefore also novel (Art.33(2) PCT).

4.5 Accordingly, also dependent claims 6-9,12,13,20-22,24-27 are novel (Art.33(2) PCT).

5 **INVENTIVE STEP** (Art.33(3) PCT)

5.1 D2 discloses the use of enzymes which hydrolyse homoserine lactone and reduce bacterial infection (see the whole article).

5.2 D1 (seen as closest prior art) focus on the production of homoserine lactone derivatives and analogues in order to treat bacterial infection by interfering with the quorum-sensing signal (mediated by homoserine lactone). Furthermore the use of antibodies binding to homoserine lactone to treat bacterial infection is also suggested (see pg.57 l.25-pg.58 l.31 and cl.52,60,61,64-67). The subject-matter of claim 1 (and dependent claims 2-4) differs from the disclosure of D1 in that the treatment of bacterial infection comprises the administration of monoclonal anti-homoserine lactone antibodies.

D1 and D2 identifies homoserine lactone as a target to treat bacterial infection. D1 suggests the use of antibodies binding to homoserine lactone to treat bacterial infection. The skilled person would have consequently a strong hint to use antibodies anti-homoserine lactone for said purpose. Therefore the only difference of the subject-matter of claim 1 from the disclosure of D1 is in the use of monoclonal antibodies. The objective remaining problem of the application is therefore to administer antibodies with higher specificity to treat bacterial infection. The solution is the use of monoclonal antibodies binding to homoserine lactone (as specified in claim 1-4). This solution is not inventive, since monoclonal antibodies can be obtained by routine methods and represent an obvious alternative to polyclonal antibodies, which merely solve a standard problem, to

be more specific and among which the skilled person would select without the exercise of any inventive skills. This solution therefore lacks inventiveness (Art.33(3) PCT).

5.3 The same arguments cited for claim 1 (and dependent claims 2-4) are valid, mutatis mutandis, for claim 17 of the application.

5.4 The subject-matter of claim 10 does also not comply with the requirements of Art.33(3) PCT, the reason being the same, mutatis mutandis, as for claim 1. In this respect it is considered that being the treatment effective for bacterial infection, there is no unexpected effect in the use of the same treatment to treat immune-suppression caused by the bacterial infection. The skilled person would see it as an obvious procedure, with reasonable expectation of success, to use the antibodies defined in claim 1-4 to treat immune suppression caused by bacterial infection. Present claim is therefore not inventive (Art.33(3) PCT).

5.5 The subject-matter of claim 19 differs from D1 (closest state of the art, see point 4.1 and 5.2 for the summary) in that the anti-homoserine lactone antibodies are monoclonal antibodies. The problem of the application is to produce antibodies with higher specificity. The solution is the provision of the monoclonal antibodies binding to homoserine lactone (as specified in claim 1). This solution cannot be considered as inventive (Art. 33(3) PCT) the reason being the same, mutatis mutandis, as under point 5.2. Monoclonal antibodies represent an obvious, straight forward alternative to polyclonal antibodies.

5.6 The same arguments cited for claim 19 are valid, mutatis mutandis, for claim 14 (the above-mentioned lack of clarity and support notwithstanding), and 32 of the application.

5.7 The subject-matter of independent claims 11,16,28-31 and 15 (the above-mentioned lack of clarity and support notwithstanding), referring to a use or compositions comprising said monoclonal antibody is also not inventive since they are mainly standard methods and products in this technical field, which fall within the routine skills of those in the art, and which do not appear to lead to any surprising effects or advantages and which are not based on an inventive step (Art.33(3) PCT).

5.8 Dependent claims 6-9,12,13,20-22,24-27 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step since they do not lead to any unexpected features or advantages.

5.9 The subject-matter of claim 33 is novel (se also point 4.4) and based on an inventive step (Art.33(3) PCT). The subject-matter of claim 33 differs from D1 (see point 4.1,5.2 for the summary), regarded as being the closest prior art, in that it refers to specific single chain antibodies produced from NCIMB-41167, NCIMB-41168, NCIMB-41169 and NCIMB-41170. The applicant is therefore the first to produce the scFv according to claim 33. Moreover, the distinguishing features, namely to be scFv and produced from the above strains, cannot be derived in an obvious way from D1. Consequently the scFv according to claim 33 are based on an inventive concept (Art.33(3) PCT).

6 The applicant is reminded that should he enter in the regional phase for the EPO, in order to comply with the provisions of the EPC the applicant should provide the examining division with the deposit receipt or any other proof of availability of the microorganism according to claim 33.

Examination of Invention II:

5,23 (completely) 1,6-19,24-32 (partially)

As for claim 1, 14 and 15 the same objections as at point 3.1 and 3.2 applies.

7 **NOVELTY** (Art.33(2) PCT)

7.1 D3 teaches the synthesis of a peptide thiolactone molecules (see fig.1) which is a signal molecule for the synthesis of virulence factors from bacteria like Staphylococcus aureus (see tab.1). Synthetic thiolactone peptide inhibit the activation of the signalling system and lesion formation caused by bacteria in a mouse protection test (see pg. 1220 right-hand column third paragraph). On the basis of these results the authors suggest that the interference with these signal molecules (peptide thiolactone) represents a new target to treat bacterial infection (see pg.1223 left-hand column last paragraph).

7.2 The subject-matter of independent claims 1 (and dependent claim 5) differs in that a monoclonal antibody binding to peptide thiolactone is administered to treat bacterial infection. In view of the available prior art the subject-matter of claims 1 and 5 appears to be novel (Art.33(2) PCT).

7.3 The same arguments cited for claim 1 applies, mutatis mutandis, for the subject-matter of independent claims 10,11,15-17,28,29-31 referring to a use or compositions comprising said monoclonal antibody and independent claims 14,19,32 referring to a

monoclonal antibody binding to peptide thiolactone, which is therefore also novel (Art.33(2) PCT).

7.4 Accordingly, also dependent claims 6-9,12,13,23-27 are novel (Art.33(2) PCT).

8 **INVENTIVE STEP** (Art.33(3) PCT)

8.1 The document D3 (see point 7.1 for the summary) is regarded as being the closest prior art to the subject-matter of claim 1 (and dependent claim 5). The subject-matter of claims 1 (and 5) differs in that the method to target the signal molecules and to treat bacterial infection comprises administering anti-peptide thiolactone monoclonal antibodies. Therefore, the problem to be solved can be seen as the use of alternative compounds. The solution is the use of anti-peptide thiolactone monoclonal antibodies. This solution does not involve an inventive step. Claims 1 (and 5) do not limit the scope to any specific monoclonal antibody, but refers to generic monoclonal antibodies binding to peptide thiolactone with no special properties other then binding to peptide thiolactone. Monoclonal antibodies represent a standard alternative to compounds binding to peptide thiolactone disclosed in D3, not leading to any unexpected properties of advantages over the prior art and among which the skilled person would choose without the exercise of any inventive skills. Therefore, the subject-matter of Independent claim 1 and dependent claim 5 appears not to be inventive (Art.33(3) PCT.

8.2 The same arguments cited for claim 1 are valid, mutatis mutandis, for claim 17 of the application.

8.3 The document D3 is regarded as being the closest prior art to the subject-matter of claim 19 (and dependent claim 23) (see point 7.1 for the summary). The subject-matter of present claims differs in that it refers to a monoclonal antibody binding to the peptide thiolactone. The problem to be solved by the present invention may therefore be regarded as providing molecules binding to the peptide thiolactone. The solution proposed, namely the monoclonal antibodies according to claim 19 cannot be considered as involving an inventive step (Art. 33(3) PCT). Since the molecule is known in the art, the production of monoclonal antibodies, binding to said molecules, is part of the common knowledge of the skilled person and cannot be consider as inventive. Inventiveness may only be acknowledged if said antibodies have special features or characteristics, beside binding to the molecule (see also point 3.1.)

8.4 The same arguments cited for claim 19 are valid, mutatis mutandis, for claim 14 and 32 of the application.

8.5 The subject-matter of independent claims 11,15,16,28-31 referring to a use or compositions comprising said monoclonal antibody is also not inventive since they are mainly standard methods and products in this technical field, which fall within the routine skills of those in the art, and which do not appear to lead to any surprising effects or advantages and which are not based on an inventive step (Art.33(3) PCT).

8.6 Dependent claims 6-9,12,13,20-22,24-27 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step since they do not lead to any unexpected features or advantages.

Examination of Invention III:

Claims 1,6-19,24-32 (all partially)

As for claim 1, 14 and 15 the same objections as at point 3.1 and 3.2 applies.

9 **NOVELTY** (Art.33(2) PCT)

9.1 D4 discloses the molecular structure of Pro-AI-2 and AI-2 (see fig.4), which act as bacterial signal molecules in gram-positive and gram-negative bacteria (see abstract).

9.2 In view of the available prior art the subject-matter of claims 1,6-19,24-32 is novel (Art.33(2) PCT).

10 **INVENTIVE STEP** (Art.33(3) PCT)

10.1 The subject-matter of claims 1,6-19,24-32 is not based on an inventive step.

10.2 The document D4 (see point 9.1 for the summary) is regarded as being the closest prior art to the subject-matter of claim 1. The subject-matter of claim 1 differs in that monoclonal antibodies binding to Pro-AI-2 or AI-2 are used to treat bacterial infection. The problem to be solved by the present invention may therefore be regarded as providing alternative targets to treat bacterial infection. Even if the prior art is silent about the use of monoclonal anti-Pro-AI-2 or AI-2 antibodies, also the application does not provide any evidence that anti-Pro-AI-2 or AI-2 antibodies would be effective for the treatment of bacterial infection. Furthermore the application does also not provide any monoclonal antibody binding to Pro-AI-2 or AI-2. Consequently, the absence of any working examples, the subject-matter of claims 1 appears not to be inventive (Art.33(3) PCT.

10.3 Also related methods and use claims 6-19,24-32 are not inventive, the reason being the same, mutatis mutandis, as for claim 1.

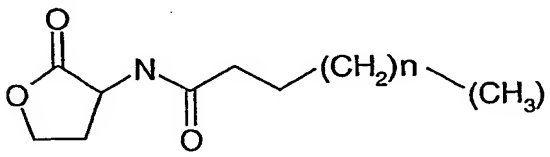
11 For the assessment of the present claims 1-10,17,18 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

CLAIMS

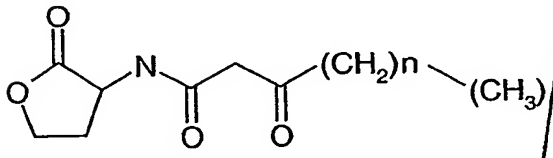
1. An antibody to a lactone or a lactone-derived signal molecule secreted by bacteria.

2. An antibody as claimed in claim 1, in which the lactone signal molecule is a homoserine molecule or a peptide thiolactone molecule.

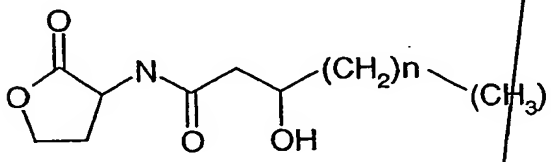
3. An antibody as claimed in claim 2, in which the homoserine lactone molecule has a general formula selected from the group consisting of:



Formula I



Formula II



Formula III

where n = 0 to 12..

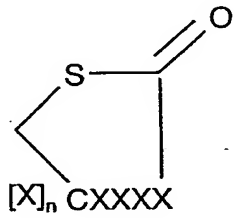
4. An antibody as claimed in claim 3, in which the homoserine lactone molecule of general formula I is *N*-butanoly-L-homoserine lactone (BHL) where n = 0, *N*-dodecanoyl-L-homoserine lactone (dDHL) where n = 8 and *n*-tetradecanoyl-L-homoserine lactone (tDHL) where n = 10.

REPLACED BY ART 34 AMDT

5. An antibody as claimed in claim 3, in which the homoserine lactone molecule of general formula II is *N*-(-3-oxohexanoyl)-L-homoserine lactone (OHHL) where n = 2 and *N*-(-3-oxododecanoyl)-L-homoserine lactone (OdDHL) where n = 8.

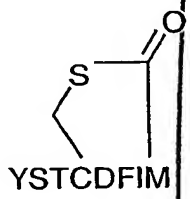
6. An antibody as claimed in claim 3, in which the homoserine lactone molecule of general formula III is *N*-(-3-hydroxybutanoyl)-L-homoserine lactone (HBHL) where n = 0.

7. An antibody as claimed in claim 2 in which the peptide thiolactone has a general formula (IV) as follows:

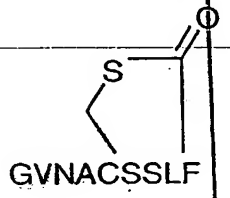


where X is any amino acid and n = 1 to 10.

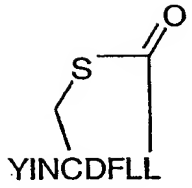
8. An antibody as claimed in claim 7, in which the peptide thiolactone molecule is:



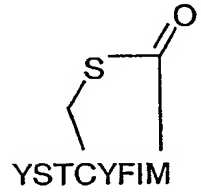
or



or

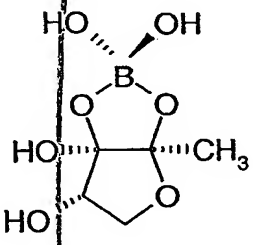


or

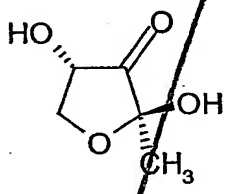


9. An antibody as claimed in claim 1, in which the lactone-derived signal molecule is a furanosyl borate diester.

10. An antibody as claimed in claim 9, in which the furanosyl borate diester is Auto Inducer-2 (AI-2),



11. An antibody as claimed in claim 1, in which the lactone-derived signal molecule is Pro-AI-2 or a C_1-C_{10} saturated or unsaturated carboxylic acid derivative thereof



12. An antibody as claimed in any one of claims 1 to 11 which is a polyclonal antibody

13. An antibody as claimed in any one of claims 1 to 11 which is a monoclonal antibody.

14. An antibody as claimed in any one of claims 1 to 11 which is a single chain antibody (scAb)

15. An antibody as claimed in any one of claims 1 to 11 which is an antibody fragment.

16. An antibody as claimed in claim 15, in which the antibody fragment is a single chain variable fragment (scFv).

17. An antibody as claimed in claim 15, in which the antibody fragment is a single domain fragment.

18. A pharmaceutical composition comprising an antibody as defined in any one of claims 1 to 17.

19. A method for the treatment of bacterial infection of a subject, the method comprising administration of an antibody as defined in any one of claims 1 to 17.

20. A kit of parts comprising an antibody as defined in any of claims 1 to 17 provided in unit dosage form.

21. An antibody as defined in any one of claims 1 to 17 for use in medicine.

22. The use of an antibody as defined in any one of claims 1 to 17 for use in the preparation of a medicament for the treatment of bacterial infection.

23. A method of screening a population of specific binding molecules for an anti-bacterial specific binding molecule, the method comprising conjugating a bacterial lactone or lactone-derived signal molecule to a carrier molecule and using the conjugate so formed to identify a specific binding molecule that specifically binds to the conjugate from the population of specific binding molecules.

24. A method as claimed in claim 23, in which the specific binding molecule is an antibody or a fragment thereof.

25. A method as claimed in claim 24, in which the antibody is a monoclonal antibody.

26. A method as claimed in claim 24, in which the antibody is a polyclonal antibody.

27. A method as claimed in any one of claims 23 to 26, in which the carrier molecule is a protein.

28. A method as claimed in any one of claims 23 to 27, in which the bacterial lactone signal molecule is a homoserine molecule or a peptide thiolactone molecule.

29. A method as claimed in any one of claims 23 to 27, in which the lactone derived signal molecule is a furanosyl borate diester, such as AI-2, or Pro-AI-2 or a C_1-C_{10} saturated or unsaturated carboxylic acid derivative thereof.

30. A method as claimed in any one of claims 23 to 29, in which the population of specific binding molecules is a phage display library.

31. A specific binding molecule identified by a method of any one of claims 23 to 30 for use in medicine.

32. The use of a specific binding molecule identified by a method according to any one of claims 23 to 30 in the preparation of a medicament for the treatment of a bacterial infection.

33. The use of a bacterial lactone or lactone-derived signal molecule to screen a population of specific binding molecules in order to identify a specific binding molecule that specifically binds to said bacterial lactone signal molecule.

34. A method of treatment of a bacterial infection of a subject, the method comprising isolation of a bacterial lactone or lactone-derived signal molecule in a sample from said subject and using said bacterial lactone signal molecule to screen a population of specific binding molecules for an anti-bacterial specific binding molecule to identify a specific binding molecule that specifically binds to the signal molecule, and administering said specific binding molecule so identified to a patient in need thereof.

35. A method as claimed in claim 34, in which the sample is of blood, saliva, tissue, cerebro-spinal fluid, tears, semen, urine, faeces, pus, skin, or mucous secretions.